

PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:)	
HSUN-LANG CHANG et al.)	Group Art Unit: 1655
Application No.: 10/552,029)	Examiner: Qiuwen Mi
Filed: October 18, 2006)	Confirmation No.: 6882
For: COMPOSITION AND METHOD)	
FOR SUPPORTING CANCER)	
TREATMENTS)	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION OF GUANG-TZUU SHANE UNDER 37 C.F.R. 1.132

I, Guang-Tzuu Shane, do hereby make the following declaration:

1. I am a citizen of Taiwan R.O.C., residing at 3F., No.2, Alley 10, Lane 96, Sec. 2, Heping E. Road, Taipei, Taiwan, R.O.C.
2. I am one of the inventors of the invention disclosed in U.S. Patent Application No. 10/552,029, which relates to a composition comprising geranium oil and extracts from the roots of *Sophora tonkinensis* and its use.
3. I graduated from National Taiwan University in 1983 with a degree in Chemistry.

4. After graduation, I worked for China Petrochemical Development Corp., as a project leader for the biological fertilizers project with a focus on licensing-in technology, developing the fertilizers, and building manufacturing plant for the fertilizers.

5. I have, in contracting out experiment work, worked with Development Center for Biotechnology and MDS Pharma Services in Taiwan in anticancer herbal medicine since 1998.

6. I have been employed by Medigreen Biotechnology Corp. since 2002 and I am currently the Vice President of Medigreen Biotechnology Corp., overseeing product research and development.

7. Animal experiments were performed in January 2003 at my instruction and under my supervision to test the efficacy of our composition comprising geranium oil and extractions of roots of *Sophora tonkinensis* in increasing blood cell count in cancer treatments. The study was performed in comparison with three other compositions: 1) AT-21, a composition comprising geranium oil and extracts from the root of *Sophora flavescens* as described by U.S. Publication No. 2003/0134003 A1 (Fong et al.), 2) a composition comprising *Sophora flavescens* powder and geranium oil extractions powder and 3) G-CSF. The experiment data was updated in June 2003 for clarification, due to an inadvertent data processing error, with respect to the G-CSF result of the January 2003 experiment which is shown in the current Application No. 10/552,029. The inadvertent error relates to data processing for two of the six tested mice. Application No. 10/552,029 shows significant increase of Lymphocyte (LY), Monocyte (MO), and Granulocyte (GR) in 5-fluorouracil (5-Fu) and G-CSF treated mice. The updated report of June 2003, with the correctly processed data, demonstrates

significant increase of White Blood Cell (WBC), MO, and GR in 5-Fu and G-CSF treated mice. The updated report of June 2003 also shows increase of LY with $p=0.057$, just falling short of significance by 0.007 with significance being $p<0.05$ in Dunnett's t-test (t-test) which is used in the study.

8. Our composition was administered orally to 24 male mice, BALB/c mice of 6-7 weeks old weighing 22 ± 2 grams, which were divided into two groups, with group 1 sacrificed on day ten and group 2 sacrificed on day fourteen. Groups 1 and 2 were further divided into two subgroups at the dosages of 7 mg/mouse/day and 21 mg/mouse/day, respectively. In the data analysis by t-test, the composition, administered orally at 7mg/mouse/day, had the significant effect of increasing the blood count of Red Blood Cell (RBC), WBC, LY, MO, and GR in mice treated with 5-Fu in comparison with the 5-Fu only control group on day ten.

9. The AT-21 composition was administered orally to 36 male mice, BALB/c mice of 6-7 weeks old weighing 22 ± 2 grams, which were divided into two groups, with group 1 sacrificed on day ten and group 2 sacrificed on day fourteen. Groups 1 and 2 were further divided into three subgroups at the dosages of 50 mg/mouse/day, 30 mg/mouse/day, and 10 mg/mouse/day respectively. The AT-21 composition, administered orally at 10 mg/mouse/day, by t-test, had the significant effect of increasing the blood count of Platelet (PLT), WBC, and LY in mice treated with 5-Fu in comparison with the 5-Fu control group on day ten.

10. The composition comprising *Sophora flavescens* powder and geranium oil extractions powder was administered orally to 24 male mice, BALB/c mice of 6-7 weeks old weighing 22 ± 2 grams, which were divided into two groups, with group 1

sacrificed on day ten and group 2 sacrificed on day fourteen. Groups 1 and 2 were further divided into two subgroups at the dosages of 7 mg/mouse/day and 21 mg/mouse/day, respectively. The *Sophora flavescens* and geranium oil composition, administered orally at 7 mg/mouse/day, by t-test, had the significant effect of increasing the blood count of MO in mice treated with 5-Fu in comparison with the 5-Fu control group on day ten.

11. The G-CSF composition was administered to 12 male mice, BALB/c mice of 6-7 weeks old weighing 22 ± 1.84 grams, which were divided into two groups, sacrificed at day ten and day fourteen respectively. The G-CSF composition was administered, by subcutaneous injection, at the dosage of 135 $\mu\text{g}/\text{mouse}/\text{day}$ for three days (day 6-8). In the updated report of June 2003, the G-CSF composition, by t-test, had the significant effect of increasing the number of WBC, MO, and GR in mice treated with 5-Fu in comparison with the 5-Fu control group on day ten.

12. In the animal experiment, day ten was when the blood count was at its lowest. For all the groups, including 5-fluorouracil treated mice and mice treated by the four compositions in this experiment, blood count on day ten was lower than blood count on day fourteen. On day ten, the animals were at the greatest risk (low white blood cells risk infection, low red blood cell will lead to anaemia, low platelets predisposes to bleeding). On day fourteen, the blood count of all the groups (including the group with 5-Fu only) was higher. The risks on day fourteen for the animals were much lower than day ten when the blood count was at its lowest. Day ten is more critical than day fourteen.

13. On day ten, the effect of oral administration of *Sophora tonkinensis* & geranium oil was better, in raising the blood count of 5-Fu treated mice, than the oral administration of *Sophora Flavescens* & geranium oil and AT-21. Also, the effect of oral administration of *Sophora tonkinensis* & geranium oil to 5-Fu treated mice had comparable effect as subcutaneous injection of G-CSF to 5-Fu treated mice, in that both increased the blood cell count of WBC, MO, and GR. The blood count of 5-Fu treated mice with orally administered *Sophora tonkinensis* & geranium oil had the significant effect, by the t-test, in raising the blood count of RBC, WBC, LY, MO, and GR. Similarly, the blood count of 5-Fu treated mice subcutaneously injected with G-CSF had the significant effect in raising the blood count of WBC, MO, and GR.

14. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: April 1, 2008

By: Home Guang-Tzuu
Guang-Tzuu Shane